MHC-Class II molecule, stimulates recognition and proliferation of $CD4^+$ cells which are specific for complexes of said polypeptide and said MHC-Class II molecule.

Claim 87: The isolated polypeptide of claim 74, consisting of an amino acid sequence found in the amino acid sequence encoded by the nucleotide sequence set forth in SEQ ID NO: 1.

REMARKS

The amendment is presented in a sincere attempt to place this application in condition for allowance or to reduce the issues on appeal. A showing of changes accompanies the amendment, and the amendments are discussed infra.

With respect to point 3, applicants reiterate that the issue regarding the declaration/power of attorney will be addressed upon allowance.

With respect to point 4, applicants submitted the '603 patent for several reasons. One of these is to show that tumor rejection antigen precursors are processed into MHC-Class II binding peptides. The examiner allowed this patent to issue, and the claims do not recited the formula of the MHC-Class II binding peptide. Written description of the binding peptide was not an issue. The '603 patent shows that the USPTO accepts the general proposition that ESO-1 is processed to Class II binders. This principle is operative here, and it is asked that the PTO follow precedent.

With respect to the written description rejection, point 5, the examiner's issue appears to be that the art does not suggest that peptides of the recited length will bind to HLA-DR53 molecules; however, it is believed that the art does show that peptides of the recited length do bind MHC-Class II molecules. For example, attached are relevant copies of pages from The HLA Facts Book showing that peptides of the relevant length do bind to Class II molecules.

The examiner has rejected claim 85, arguing that there is no support for claims that encompass the peptide of SEQ ID NO: 7, plus one of the peptides of claim 74.

Page 37 of the specification describes the peptide of SEQ ID NO: 7, which binds to HLA-A2-Class I molecule. Page 38 then discusses the peptides of claim 74. At page 38, line 16, the specification states:

> "(O)ne may combine both types of peptide, such as in immune compositions, thereby generating a combined immune response. Hence, all applications described can be used with just the Class I restricted peptides, with just the Class II restricted peptides, or with combinations of these."

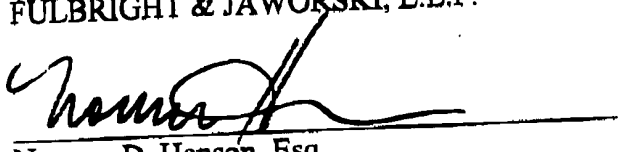
Also, please refer to originally filed claims 55-60, which constitute original disclosure. Hence, the subject matter of claim 85 can hardly be deemed to constitute new matter.

Finally, with respect to the rejection of claim 87, the claim has been amended to refer to a polypeptide which has an amino acid sequence that is found in the protein encoded by SEQ ID NO: 1. This should address the issue

All issues have been addressed. Allowance of this application is believed proper and is urged.

Respectfully submitted,

FULBRIGHT & JAWORSKI, L.L.P.



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THE HLA *FactsBook*

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DRB1*01 – DR1, DR103

Alleles

Alleles	Serological specificity	Cells sequenced	EG	Ethnic origin of sequenced cells	Accession number	Refs
DRB1*0101	DR1	LG2	Unk	Unknown	M11161	1
		45.1	Unk	Unknown	X03069	2
		JSA	Cau	Mexico, North America	AF029288	
		DRH	Cau	Mexico, North America	AF029288	
		CHG	Cau	Mexico, North America	AF029288	
DRB1*01021	DR1	NASC	Unk	Unknown	–	3
		1568	Blk	African American, North America	M21008	4
		MUM	Cau	Mexico, North America	AF029293	
DRB1*01022	DR1	TO0973	Cau	Unknown	Z50871	5
DRB1*0103	DR103	TER-ND	Cau	Ireland, Europe	–	6
		BON	Cau	France, Europe	M33600	7
		BG	Unk	Unknown	–	8
DRB1*0104	DR1	LAUTH J	Cau	Unknown	X70261	9
		LAUTH J	Cau	Unknown	X99896	
DRB1*0105	?	JC10218	Ori	Japan, Asia	AB015184	
DRB1*0106	?	MGM14106	Cau	Spain, Europe	AJ089723	

Population distribution

Major ethnic group	Average frequency (%)	Range of frequency (%)
Black	5.46	0.00–9.20
Caucasoid	9.42	4.50–26.20
Oriental	2.98	0.00–16.10
Amerindian	1.50	0.70–2.30
Australasian Aboriginals	NA	NA

Peptide-binding specificity

Allotype/ serotype	Peptide sequence	Source protein	Refs
DRB1*0101			
Motif	Relative position 1 2 3 4 5 6 7 8 9 Y L A L F M G A W A S I L I T V I V C M M M P F V Y A M W		10–12
Endogenous peptides	STPEFTILNTFHIPSFTI	Apolipoprotein B 2646–2663	13
	LDHKFDLMYAKRAFVHWY	Tubulin α 1 chain 391–408	13
	YKHTLNQIDSVKVWPRRPT	Bovine fetuin 56–74	14
	[illegible]	Bovine fetuin 56–73	14
	LPKPPKPVSKMRMATPLLMQALPMG	Invariant chain 81–105	15

Allotype/ serotype	Peptide sequence	Source protein	Refs
	LPKPPKPVSKMRMATPLLMQALPM	Invariant chain 81–104	14
	LPKPPKPVSKMRMATPLLMQALP	Invariant chain 81–103	14
	LPKPPKPVSKMRMATPLLMQAL	Invariant chain 81–102	13
	PKPPKPVSKMRMATPLLMQALPMG	Invariant chain 82–105	14
	PKPPKPVSKMRMATPLLMQALPM	Invariant chain 82–104	14
	PKPPKPVSKMRMATPLLMQALP	Invariant chain 82–103	14
	KPPKPVSKMRMATPLLMQALPM	Invariant chain 83–104	14
	KPPKPVSKMRMATPLLMQALP	Invariant chain 83–103	14
	PPKPVSKMRMATPLLMQALP	Invariant chain 84–103	14
	KMRMATPLLMQALPM	Invariant chain 90–104	14
	KMRMATPLLMQALP	Invariant chain 90–103	14
	VGSDWRFLRGYHQYAYDG	HLA-A2 103–120	14
	VGSDWRFLRGYHQYA	HLA-A2 103–117	14
	VGSDWRFLRGYHQY	HLA-A2 103–116	14
	GSDWRFLRGYHQYA	HLA-A2 104–117	14
	SDWRFLRGYHQYA	HLA-A2 105–117	14
	IPADLRIISANGCKVDNS	(Na^+/K^+) ATPase 199–216	14
	RVEYHFLSPYVSPKESP	Transferrin receptor 680–696	14
	LATWTIQGAANALSGDVW	Transferrin receptor 737–754	13
	HPNQPFYILKPQMPWELW	Sialyltransferase 288–305	13
	AILEPRAMAQFSRKTD	Unknown	15
T-cell epitopes	PKYVKQNTLKLA	Influenza haemagglutinin 307–318	16
	GPLKAEIAQRLE	Influenza matrix protein 18–29	16
DRB1*0102			
Motif	Relative position 123456789 I A A I L L G L V M S A M T M C Y P W		13
Endogenous peptides	YIPHVMAYAACIGANRDH	Alkaline phosphatase 479–496	13
	LPKPPKPVSKMRMATPLLMQAL	Invariant chain 81–102	13
	DLNPLIKLSGAYLVDDSD	Mannose-6-phosphate receptor 185–202	13
	LPNIPVQTISRAAAEKLF	Transferrin receptor 332–349	13
	IFVKTLTGKTITLEVEPS	Ubiquitin 3–20	13
	SPNIVIALSGNKADLANK	Ras-related protein Rab-5A 123–140	13
DR1			
T-cell epitopes	REEAYHAA	Ragweed allergen E 54–61	16
	TSLYNLRRGTALA	EBV EBNA1 515–527	17
	GNNDNVLDHLTQR	Pertussis toxin S1 subunit 27–39	18
	HQSLVIKLMPNITLL	Measles virus fusion protein 51–65	19
	QVIKANSKFIGITEL	Tetanus toxin 830–844	20
	AVLEDPYILLVSSKV	*M. tuberculosis* 65-kDa protein 211–225	21
	QNLLKAEKGNKAAQR	*Chlamydia* histone-like protein Hc 1 19–34	22
	GRETVIEYLVSFGVW	HBV nucleocapsid protein 111–125	23
	VSFGVWIRTPPAYRPPNAPI	HBV nucleocapsid protein 120–139	24
	EYLNKIQSLSTEWSPCS	*P. falciparum* circumsporozoite 326–343	25
	TGKENTIKIQEGSGLSKEEI	*M. leprae* HSP70 468–487	26
	DIEKKIAKMEKASSVFNVVNS	*P. falciparum* circumsporozoite 378–398	27
	TRANPNPYTSRRSVASIVGTLVRM	Pertussis toxin S1 subunit 171–194	18

Peptide-binding specificity

Allotype/ serotype	Peptide sequence	Source protein	Refs
DRB1*0301			
Motif	Relative position		
	123456789		
	L D K LY		16
	I R L		
	F E F		
	M Q		
	V N		
Endogenous peptides	VDTFLEDVKNLYHSEA	α_1-antitrypsin 149–164	16
	YFNPIMDPKELDKV	Unknown	16
	KQTISPDYRNMI	IgG2a	16
	ISNQLTLDSNTKYFHKLN	Bovine apolipoprotein B 2877–94	16
	ISNQLTLDSNTKYFHKL	Bovine apolipoprotein B 2877–93	16
	ISNQLTLDSNTKYFHK	Bovine apolipoprotein B 2877–92	16
	KPRAIVVDPVHGFMY	LDL receptor 518–532	16
	NIQLINDQEVARFD	Unknown	16
DRB1*0301 or DRB3*0201			
Motif	Relative position		
	1234		
	F D		17
	I N		
	L Q		
	V T		
	Y		
Endogenous peptides	PPEVTVLTNSPVELREPNV	HLA-DR α chain 111–129	17
	PPEVTVLTNSPVELREPN	HLA-DR α chain 111–128	17
	ATKYGNMTEDHVMHLLQNA	Invariant chain 115–133	17
	VFLLLLADKVPETSLS	Acetylcholine receptor 289–304	17
	YGYTSYDTFSWAFL	Na⁺ channel protein 384–397	17
	GQVKKNNHQEDKIE	CD45 1071–1084	17
	LNKILLDEQAQWK	ICAM-2 64–76	17
	GPPKLDIRKEEKQIMIDIFHP	IFNγ receptor 128–148	17
	GPPKLDIRKEEKQIMIDIFH	IFNγ receptor 128–147	17
	KELKRQYEKKLRQ	EBV tegument p140 1395–1407	17
	SPLQALDFFGNGPPVNYKTGNL	IP-30 38–59	17
	SPLQALDFFGNGPPVNYKTG	IP-30 38–57	17
	GKFAIRPDKKSNPIIRTV	NADH-cytochrome b5 reductase 155–172	17
	IPDNLFLKSDGRIKYTLNKN	Bovine apolipoprotein B-100 1273–1292	17
	IPDNLFLKSDGRIKYTLNK	Bovine apolipoprotein B-100 1273–1291	17
	IPDNLFLKSDGRIKYTLN	Bovine apolipoprotein B-100 1273–1290	17
	IPDNLFLKSDGRIKYTL	Bovine apolipoprotein B-100 1273–1289	17
	NLFLKSDGRIKYTLNKNSLK	Bovine apolipoprotein B-100 1276–1295	17
	NLFLKSDGRIKYTLNK	Bovine apolipoprotein B-100 1276–1291	17
	NLFLKSDGRIKYTLN	Bovine apolipoprotein B-100 1276–1290	17
	YANILLDRRVPQTDMTF	Bovine apolipoprotein B-100 1207–1224	17
	VTTLNSDLKYNALDLTN	Bovine apolipoprotein B-100 1794–1810	17
	TFDEIASGFRQGGASQ	Glucose transporter 459–474	17
	TGHGARTSTEPTTDY	EBV gp220 592–606	17

Alleles	Serological specificity	Cells sequenced	EG	Ethnic origin of sequenced cells	Accession number	Refs
DRB1*0417	DR4	TOB-0070	Ami	Toba, Argentina, South America	L14481	23
DRB1*0418	?	AI7	Cau	India, Asia	X71610	24
		AI8	Cau	India, Asia	X71610	24
		74DR	Unk	Unknown	U38974	
DRB1*0419	DR4	FK	Cau	Unknown	L21985	25
DRB1*0420	DR4	AD-7863	Cau	England, Europe	L27217	26
		BM29/92	Unk	Unknown	L27217	26
DRB1*0421	DR4	SMH	Cau	Unknown	X80288	27
DRB1*0422	DR4	D18002	Cau	Unknown	U17014	28
DRB1*0423	DR4	MAG	Cau	Unknown	Z68503	29
DRB1*0424	DR4	M.i	Cau	France, Europe	Z71541	30
DRB1*0425	DR4	RJ	Blk	Aruba, West Indies	Y09211	
		HB	Blk	Aruba, West Indies	Y09211	
DRB1*0426	DR4	T010148	Cau	Unknown	AJ001252	31
DRB1*0427	?	NOR03	Unk	Unknown	AF030439	
DRB1*0428	DR4	JC6772	Ori	Japan, Asia	AB007635	
DRB1*0429	DR4	JC7616	Ori	Japan, Asia	AB007636	
DRB1*0430	?	JC9227	Ori	Japan, Asia	AB015185	
DRB1*0431	?	GE47192	Unk	Unknown	AJ009755	
DRB1*0432	?	NIE	Cau	Unknown	Y17273	

Population distribution

Major ethnic group	Average frequency (%)	Range of frequency (%)
Black	10.51	1.90–43.50
Caucasoid	12.82	5.20–24.80
Oriental	12.99	4.10–22.80
Amerindian	40.00	38.30–41.70
Australasian Aboriginals	NA	NA

Peptide-binding specificity

Allotype/ serotype	Peptide sequence	Source protein	Refs
DRB1*0401			
Motif	Relative position 123456789 P M L Q V S T		32
Endogenous peptides	VDDTQFVRFDSDAASQRMEPRAP	HLA-A2 28–50	32
	VDDTQFVRFDSDAASQRMEPR	HLA-A2 28–48	32
	VDDTQFVRFDSDAASQRMEP	HLA-A2 28–47	32
	VDDTQFVRFDSDAASQRME	HLA-A2 28–46	32
	VDDTQFVRFDSDAASQR	HLA-A2 28–44	32
	DTQFVRFDSDAASQRMEPR	HLA-A2 30–48	32
	TQFVRFDSDAASQRMEPRA	HLA-A2 31–49	32

Allotype/ serotype	Peptide sequence	Source protein	Refs
	IQAEPYLNPDQSQEFMFD	HLA-DR α chain 33–50	17
	VIDWLVSNQSVRNRQEGL	Pleckstrin 161–178	17
	KSSVITLNTNAELFNQSD	Apolipoprotein 3344–3361	17
DRB3*0301			
Motif	Relative position 123456789 I N A I L S L V P V D E		17
Endogenous peptides	AQVIILNHPGQISAGYAP	Elongation factor Tu 342–359	17
	VPPEVTVLTNSPVELREP	HLA-DR α chain 110–127	17
	FPPSSEELQANKATLVCL	Ig lambda chain 11–28	17
T-cell epitope	TPQLTKNAGVLT	Japanese cedar pollen allergen *Cry j*1 335–346	18
DR52a			
T-cell epitopes	GQIGNDPNRDIL	Tetanus toxin 1273–1284	19,20
	QYIKANSKFIGITEL	Tetanus toxin 830–844	19
	ESWGAVWRIDTPDKLTGPFT	Pollen allergen *Lol p* 1 191–210	21
DR52b			
T-cell epitope	QYIKANSKFIGITEL	Tetanus toxin 830–844	19
DR52c			
T-cell epitope	GQIGNDPNRDIL	Tetanus toxin 1273–1284	19

Amino acid sequence

DRB3*0101

```
-29 .......... .......... ..........
  1 GDTRPRFLEL RKSECHFFNG TERVRYLDRY FHNQEEFLRF DSDVGEYRAV
 51 TELGRPVAES WNSQKDLLEQ KRGRVDNYCR HNYGVGESFT VQRRVHPQVT
101 VYPAKTQPLQ HHNLLVCSVS GFYPGSIEVR WFRNGQEEKA GVVSTGLIQN
151 GDWTFQTLVM LETVPRSGEV YTCQVEHPSV TSALTVEWRA RSESAQSKML
201 SGVGGFVLGL LFLGAGLFIY FRNQKGHSGL QPTGFLS
```

DRB4 – DR53

Alleles

Alleles	Serological specificity	Cells sequenced	EG	Ethnic origin of sequenced cells	Accession number	Refs
DRB4*01	DR53	LBF	Cau	England, Europe	M17385, M17388	1
		LKT3	Ori	Japan, Asia	M15071	2
		FS	Unk	Unknown	M15071	2
		BURKHARDT	Unk	Unknown	–	3
		PRIESS	Cau	Denmark, Europe	K02775	4
		DM24	Unk	Unknown	–	5
		DM29	Unk	Unknown	–	5
		MMCC	Unk	Unknown	–	6
DRB4*01011	DR53	MOU	Cau	Denmark, Europe	M16942	7
DRB4*0101102N: *Name abandoned*						
DRB4*0102	?	C.M.L.	Cau	Belgium, Europe	L08621	8
		C.M.L.	Cau	Belgium, Europe	D89879	9
DRB4*0103101	DR53	ROLETH	Cau	Sweden, Europe	M20555	10
		MJ4	Unk	Unknown	M15178, M15179	11
		DKB	Cau	Netherlands, Europe	M17385, M17388	1
		HSF7	Unk	Unknown	Z84477	
DRB4*0103102N	Null	DBB	Cau	Amish, North America	–	12
		DBB	Cau	Amish, North America	D89918	9
DRB4*01032	DR53	W778R	Cau	Unknown	AF048707	
DRB4*0104	?	69–218	Cau	Unknown	X92712	13
		76–394	Cau	Unknown	X92712	13
DRB4*0105	DR53	17345	Cau	Unknown	Y09313	14
DRB4*0201N	Null	GN016	Cau	Germany, Europe	U50061, U70543, U70544	15
DRB4*0301N	Null	GN017	Cau	England, Europe	U70542	15

Population distribution

Not available.

Peptide-binding specificity

Allotype/ serotype	Peptide sequence	Source protein	Refs
DRB4*0101			
	Motif not characterized		
Endogenous peptide	NNAKYAISMARKIGA	L-plastin 581–595	16
DR53			
T-cell epitopes	PISLERLDVG	Measles virus fusion protein 454–463	17
	IEQYLEKKIKNSISTEWSPC	*P. falciparum* circumsporozoite 331–350	18

VIA FACSIMILE

I hereby certify that this correspondence is being facsimile transmitted to the U.S. Patent and Trademark Office on May 7, 2002.

FULBRIGHT & JAWORSKI LLP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Alexander, et al.
Serial No	:	09/165,546
Filed	:	October 2, 1998
For	:	ISOLATED PEPTIDES CORRESPONDING TO AMINO ACID SEQUENCES OF NY-ESO-1...
Art Unit	:	1644
Examiner	:	A. Decloux

May 7, 2002

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

SHOWING OF CHANGES

Claim 74: (Amended) An isolated polypeptide which binds to an MHC-Class II [HLA-DR53] molecule[s], said polypeptide comprising [which comprises] at least 18 and no more than 25 amino acids, said polypeptide further comprising [having at least one HLA-DR53 binding] a motif [, said motif] consisting of four amino acids, wherein the first amino acid is Tyr, Phe, Trp or Leu, and the fourth amino acid is Ala or Ser, wherein said polypeptide, when bound to said MHC-Class II molecule, stimulates recognition and proliferation of $CD4^+$ cells which are specific for complexes of said polypeptide and [HLA-DR53] said MHC-Class II molecule.

Claim 87: (Amended) The isolated polypeptide of claim 74, consisting of an amino acid sequence found in the amino acid sequence encoded by the nucleotide sequence set forth in SEQ ID NO: 1.

Respectfully submitted,

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